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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|

| EXAMINER | |
|---|---|
| ART UNIT | PAPER NUMBER |

DATE MAILED:

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 08/803,702 | Maino et al. |
| **Examiner** | **Art Unit** |
| G. R. Ewoldt | 1644 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) [X] Responsive to communication(s) filed on *Aug 1, 2001* .

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) [X] Claim(s) *19-55 and 61-63* is/are pending in the application.

4a) Of the above, claim(s) *22, 34-38, 41, 42, 44, 46, and 48* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *19-21, 23-33, 39, 40, 43, 45, 47, 49-55, and 61-63* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) [ ] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other: _____

**DETAILED ACTION**

1. Claims 19-21, 23-33, 39-40, 43, 45, 47, 49-55, and 61-63 are being acted upon.

2. In view of Applicant's amendment and response, and declaration of Calman Prussin, M.D., filed 8/01/01, only the following rejections remain. Note that the declaration of Calman Prussin, M.D., has been rendered moot as the enablement rejection which it addresses has been withdrawn.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 19-21, 23-33, 40, 43, 45, 47, 49-55, and 61-63 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention for the reasons set forth in Paper No. 24, mailed 1/30/01.

Applicant's arguments, filed 8/01/01, have been fully considered but they are not persuasive. Applicant argues that one skilled in the art would have recognized that Applicants were in possession of the claimed methods as practiced with either BFA or with monensin because others working in the field at the time of the invention published similar work employing monensin as an inhibitor of cytokine secretion. However, regardless of what Applicant asserts one of skill in the art would have reasonably believed, no inhibitors of cytokine secretion other than BFA are disclosed in the specification, thus, an insufficient number of said inhibitors have been described to support the generic claims.

5. The instant application is Continuation in Part of Application No. 08/760,447 (12/6/96) and claims priority to said application. However, due to significant differences between the disclosures of the two applications, priority is denied.

Applicant's arguments, filed 8/01/01, have been fully considered but they are not persuasive. Applicant argues that Figures 1-4 fully support the claimed invention because said

figures "report the frequencies of effector T cells." Applicant further argues that the Examiner does not have the legal authority to assert that the incubation time disclosed in the instant application is critical, and regardless, "the '447 clearly discloses antigen incubation of 6-24 hours." Regarding, Figures 1-4, i.e., the asserted display of individual cytometric events, it is the Examiner's position that the '447 application does not disclose a method aimed at collecting data from individual cells, as the application discloses only T cells as a subpopulation in a larger purified PBMC population. Further, it is the Examiner's position that said figures do not display individual, discrete, dots (representing individual events), nor are they meant to. Regarding the timing of incubation, Applicant is referred to page 3, line 27 of the '447 specification which discloses a culture time of 101.5 hours. Applicant's assertion, nearly 6 years post-filing, that a key element of the invention is now a typographical error, can not be found persuasive. It is the Examiner's position that Applicant had not envisaged the instant invention, including all the claimed limitations, such as the use of whole blood (instant Claim 1) instead of purified PBMC, at the time of filing of the '447 application.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 19-21, 23-33, 39-40, 43, 45, 47, 49-55, and 61-63 stand rejected under 35 U.S.C. 103(a) as being unpatentable Becton Dickinson Application Note 1, Detection of Intracellular Cytokines in Activated Lymphocytes (1996) in view of Maino et al. (FastImmune™ Assay System, 1995, IDS), and, U.S. Patent No. 6,143,299, all of record, for the reasons set forth in Paper No. 24, mailed 1/30/01.

Applicant's arguments, filed 6/18/01, have been fully considered but they are not persuasive. Applicant argues that the Application Note 1 reference describes no more than the Picker et al. reference, rejections over which have been withdrawn. Applicant argues that the Picker et al. reference can not provide sufficient motivation for it to be combined with the Maino et al. reference. Applicant argues that said motivation would have been absent due to a lack of expectation of success.

Applicant argues that said lack of expectation of success would have been due to too few antigen-activated cells to be detected. However, unlike the Picker et al. reference, the Application Note 1 reference was written specifically as a method for using the FastImmune™ Assay System described by Maino et al. It is the Examiner's position that the Maino et al. reference provides a sufficient expectation of success. The reference teaches that individual antigen-activated cells are detectable (particularly in light of Applicant's argument that flow cytometry measures only individual events, i.e., individual cells, see Applicant's arguments regarding Priority). The Application Note 1 reference teaches additional claimed limitations, i.e., the measure of intracellular cytokines (the value of which Applicant has not argued) for a product already publicly available. Given the addition of costimulation (to boost activation) and the addition of BFA (to inhibit cytokine secretion and thus, boost signal) in addition to the teaching of the Maino et al. reference that individual antigen-activated cells can indeed be cytometrically assayed, one of skill in the art at the time of the invention would have had a reasonable expectation of success in performing the claimed method with nothing more than routine optimization.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321c may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 10-15, 17, 19, 24-36, and 39 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 10-15, 17, 19, 23, 25-35 and 39 of copending Application No. 09/526,253. Although the conflicting claims are not identical,

they are not patentably distinct from each other because both applications recite claims drawn to a method of detecting antigen-specific lymphocytes comprising flow cytometrically detecting a cytokine and a T cell subset in the presence of a protein synthesis inhibitor. Note that at the time of the restriction of the '702 application the claims of said application were drawn to a method of detecting antigen-specific cytokine production. Subsequent amendment of the claims of the '702 application has necessitated this rejection. Further note that the claims of the '702 application are drawn to "an MHC-dependent nominal antigen" while the claims of the '253 application are drawn to a "vaccine antigen". However, neither antigen is defined in the specifications and said antigens are not considered to be patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection has been traversed but no specific arguments have been submitted.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist

whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Patrick J Nolan

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
August 27, 2000

Patrick J. Nolan, Ph.D.
Primary Examiner
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